

AMENDMENTS TO THE SPECIFICATION

Please amend the specification as follows.

Please replace the paragraph starting on page 4, lines 19 with the following paragraph:

U.S. Patent Application Publication No. US 2002/~~016216~~ 0162126 discloses a method for attenuating expression of a target gene in cultured cells by introducing double stranded RNA (dsRNA) that comprises a nucleotide sequence that hybridizes under stringent conditions to a nucleotide sequence of the target gene into the cells in an amount sufficient to attenuate expression of the target gene.

Please replace the paragraph starting on page 36, line 9 with the following paragraph:

Preferably, the performance of the obtained PSSM is evaluated. In one embodiment, the PSSM is evaluated using an ROC (receiver operating characteristic) curve. An ROC curve is a plot of the sensitivity of a diagnostic test as a function of non-specificity. An ROC curve indicates the intrinsic properties of a test's diagnostic performance and can be used to compare relative merits of competing procedures. In one embodiment, the sensitivity of a PSSM is calculated as the proportion of true positives detected as a fraction of total true positives, whereas the non-specificity of the PSSM is calculated as the proportion of false positives detected as a fraction of total false positives (see, e.g., Campbell G. Chambers, 1994, Statistics in Medicine 13:499–508; Metz, 1986, Investigative Radiology 21:720–733; Gribskov et al., 1996, Computers Chem. 20:25–33). FIG. 3 shows ROC curves of the two PSSMs selected for the current best practice of the invention.

Please replace the paragraph starting on page 68, line 17 with the following paragraph:

The siRNAs can also be delivered to an organ or tissue using a gene therapy approach. Any of the methods for gene therapy available in the art can be used to deliver the siRNA. For general reviews of the methods of gene therapy, see Goldspiel et al., 1993, Clinical Pharmacy 12:488-505; Wu and Wu, 1991, Biotherapy 3:87-95; Tolstoshev, 1993, Ann. Rev. Pharmacol. Toxicol. 32:573-596; Mulligan, 1993, Science 260:926-932; and

Morgan and Anderson, 1993, Ann. Rev. Biochem. 62:191-217; Robinson May, 1993, TIBTECH 11(5):155-215). In a preferred embodiment, the therapeutic comprises a nucleic acid encoding the siRNA as a part of an expression vector. In particular, such a nucleic acid has a promoter operably linked to the siRNA coding region, in which the promoter being inducible or constitutive, and, optionally, tissue-specific. In another particular embodiment, a nucleic acid molecule in which the siRNA coding sequence is flanked by regions that promote homologous recombination at a desired site in the genome is used (see e.g., Koller and Smithies, 1989, Proc. Natl. Acad. Sci. U.S.A. 86:8932-8935; Zijlstra et al., 1989, Nature 342:435-438).

Please replace the paragraph starting on page 70, line 24, with the following paragraph:

Effects of gene silencing on a cell can be evaluated by any known assay. For example, cell growth can be assayed using any suitable proliferation or growth inhibition assays known in the art. In a preferred embodiment, an MTT proliferation assay (see, e.g., van de Loosdrechet, et al., 1994, J. Immunol. Methods 174: 311-320; Ohno et al., 1991, J. Immunol. Methods 145:199-203; Ferrari et al., 1990, J. Immunol. Methods 131: 165-172; Alley et al., 1988, Cancer Res. 48: 589-601; Carmichael et al., 1987, Cancer Res. 47:936-942; Gerlier et al., 1986, J. Immunol. Methods ~~65~~ 94:55 57-63; Mosmann, 1983, J. Immunological Methods 65:55-63) is used to assay the effect of one or more agents in inhibiting the growth of cells. The cells are treated with chosen concentrations of one or more candidate agents for a chosen period of time, e.g., for 4 to 72 hours. The cells are then incubated with a suitable amount of 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) for a chosen period of time, e.g., 1-8 hours, such that viable cells convert MTT into an intracellular deposit of insoluble formazan. After removing the excess MTT contained in the supernatant, a suitable MTT solvent, e.g., a DMSO solution, is added to dissolve the formazan. The concentration of MTT, which is proportional to the number of viable cells, is then measured by determining the optical density at e.g., 570 nm. A plurality of different concentrations of the candidate agent can be assayed to allow the determination of the concentrations of the candidate agent or agents which causes 50% inhibition.

Please add the following new paragraph after Table IV on page 104:

This application includes a Sequence Listing submitted on compact disc, recorded on two compact discs, including one duplicate, containing Filename SEQLIST 9301-244-999.TXT, of size 210 kilo-bytes, created March 12, 2007. The Sequence Listing on the compact discs is incorporated by reference herein in its entirety.

Please amend the specification to insert the Sequence Listing submitted herewith.